

	PAT-NO	ISSUE-DATE	PATENTEE-NAME	US-CL
<input type="checkbox"/>	<u>4474893</u>	October 1984	Reading	
<input type="checkbox"/>	<u>4722899</u>	February 1988	Hamaoka et al.	
<input type="checkbox"/>	<u>4752582</u>	June 1988	Vanderlaan et al.	
<input type="checkbox"/>	<u>4868109</u>	September 1989	Lansdorp	
<input type="checkbox"/>	<u>5087570</u>	February 1992	Weissman et al.	
<input type="checkbox"/>	<u>5137809</u>	August 1992	Loken et al.	
<input type="checkbox"/>	<u>5262319</u>	November 1993	Iwata et al.	

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ART-UNIT: 162

PRIMARY-EXAMINER: Burke; Julie

ATTY-AGENT-FIRM: Bereskin & Parr

ABSTRACT:

The present invention relates to antibody composition that are useful in

preparing enriched cell preparations such as human hematopoietic progenitor cells and stem cells and non-hematopoietic tumor cells. The invention also relates to kits for carrying out the processes and to the cell preparations prepared by the processes.

11 Claims, 9 Drawing figures

Detailed Description Paragraph Center (18):Enrichment of Breast Carcinoma Cells in Peripheral BloodDetailed Description Paragraph Table (5):

TABLE 4

Antibodies Recognizing Non-Hematopoietic Antigens Expressed on Epithelial Tumor Cells.
Disease Antibody Antigen Supplier/Developer

	Breast and
Lung 5E11 unknown, breast carcinoma STI Carcinoma 6E7 unknown, breast carcinoma STI	
H23A unknown, breast carcinoma ATCC RAR9941 epithelial glycoprotein Baxter, Germany	
RAR9948 epithelial glycoprotein Baxter, Germany RAR9938 crb2 Baxter, Germany C13B5 crb2	
Immunotech, Marseille, France BRST 1 BCA 225 ID Labs BRST 3 TAG-72 ID Labs CA15.3	
MAM-6, mucin ID Labs CA27.29 MAM-6, mucin Cedarlane BcrEp4 HEA DAKO Neuroblastoma UJ13A	
unknown Hurko and Walsh (1983) Neurology 33:734 UJ181.4 unknown Hurko and Walsh (1983)	
Neurology 33:734 UJ223.8 unknown Hurko and Walsh (1983) Neurology 33:734 UJ127.11	
unknown Hurko and Walsh (1983) Neurology 33:734 5.1.H11 unknown Hurko and Walsh (1983)	
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unknown R. C. Seeger, L.A. Children's Hospital, Calif. HSN 1.2 unknown Reynolds and	
Smith (1982) Hybridomas in Cancer p235	

Detailed Description Paragraph Table (8):

TABLE 7

Purging Breast Carcinoma Cells (BT20 or T47D cells). Anti-Breast Carcinoma Log Tumor
Cell Cell Type Lineage Depletion Antibodies Depletion

	Previously
Frozen Bone Purge Only 5E11 1.8 Marrow 5E11, H23A 3.7, 3.7 5E11, 6E7 3.0	Previously
Frozen Bone Lineage Depletion and Purge 5E11 >5.8, 3.9, 4.7 Marrow RAR >5.8, 4.3, 4.7	
BRST1 4.9 5E11, H23A >5.2, 4.4 5E11, RAR, BRST1 >5.8 Peripheral Blood Purge only 5E11	
1.9, 1.9 Leukapheresis H23A 1.7 5E11, H23A 2.3 Peripheral Blood Lineage Depletion and	
Purge 5E11, H23A 5.6 Leukapheresis Fresh Bone Marrow Lineage Depletion and Purge 5E11,	
H23A 4.6, 4.4	

Detailed Description Paragraph Table (10):

TABLE 9

Enrichment of CAMA Breast Carcinoma Tumor Cells From Bone Marrow # CAMA in % CAMA in %
CAMA in % Recovery Log Enrich. Exp # Sample Start Start Flow CAMA CAMA

	1 BM
1.1/10.sup.2 1.06 91.07 72.41 1.9 2 BM 2.2/10.sup.2 2.18 96.40 44.12 1.6 2.1/10.sup.3	
0.21 82.16 75.00 2.6 2.1/10.sup.4 0.02 32.01 60.00 3.2 3 BM 2.6/10.sup.3 0.26 62.54 *	
2.4 2.6/10.sup.4 0.026 11.21 * 2.6 2.6/10.sup.5 0.0026 2.01 * 2.9 2.6/10.sup.6 0.00026	
0.13 * 2.7	

*Cell numbers were too low to count accurately.

Detailed Description Paragraph Table (11):

TABLE 10

Purity, Recovery, and Enrichment of
CAMA Breast Carcinoma Tumor Cells Seeded into Previously Frozen Peripheral Blood
Mononuclear Cells Start Enriched Fraction % Purity % Recovery Log Enrichment

	0.3	95.5	9.0	2.5	0.03	65.3	13.3	3.4	0.003	17.1
12.1 3.8 0.3 96.7 14.3 2.5 0.03 52.4 13.1 3.3 0.003 82.7 14.8 4.5 0.3 92.7 25.8 2.5										
0.03 61.4 17.0 3.3 0.003 16.8 7.0 3.7 0.3 91.2 14.5 2.5 0.03 61.3 17.9 3.3 0.003 18.0										
8.0 3.8 0.02 24.5 47.2 3.1 0.02 9.3 42.9 2.7 0.1 97.7 85.8 2.9 0.01 81.0 86.1 3.9 0.001										
21.4 62.1 4.3 0.004 6.6 4.4 3.2 0.03 42.8 12.5 3.2 0.02 35.7 12.8 3.3 0.01 40.4 62.3										
3.5 0.01 36.3 54.2 3.4 0.01 33.7 53.0 3.4 0.02 43.3 25.2 3.4 0.02 52.9 38.1 3.5 0.02										
26.9 113.0 3.2 0.02 34.7 71.9 3.3										

Detailed Description Paragraph Table (12):

TABLE 11

Purity and Enrichment of CAMA Breast
Carcinoma Tumor Cells Seeded into Previously Frozen Peripheral Blood Mononuclear Cells:
Antibody Composition of the Invention vs. CD45 Depletion Only Start Enriched Fraction
Cocktail % Purity % Purity Log Enrichment

	0.001	21.4	4.3	Anti-CD45 only	0.001	6.2	3.8	Antibody Cocktail	0.03
42.8 3.2 Anti-CD45 only 0.03 6.6 2.4 Antibody Cocktail 0.02 35.7 3.3 Anti-CD45 only									
0.02 5.4 2.4 Antibody Cocktail 0.01 40.4 3.5 Anti-CD45 only 0.01 11.8 3.0 Antibody									
Cocktail 0.01 36.3 3.4 Antibody Cocktail 0.01 33.7 3.4 Anti-CD45 only 0.01 8.0 2.8									
Antibody Cocktail 0.02 43.3 3.4 Anti-CD45 only 0.02 20.1 3.1 Antibody Cocktail 0.02									
26.9 3.2 Antibody Cocktail 0.02 34.7 3.3 Anti-CD45 only 0.02 3.5 2.3									

Detailed Description Paragraph Right (30):

A preferred antibody composition for removing differentiated hematopoietic cells and breast and lung carcinoma cells from a sample comprises the monoclonal antibodies 2B7.1 (glycophorin A), SK7 (CD3), MEM15 (CD14), 3G8 (CD16), ALB9 (CD24), 80H3 (CD66b), J4.119 (CD19), 6F10.3 (CD2), MY31 (CD56), or the monoclonal antibodies 10F7MN (glycophorin A), SK7 (CD3), 32D12 (CD24), MEM154 (CD16), MEM15 (CD14), 80H3 (CD66b) or B13.9 (CD66b), T199 (CD56), 6F10.3 (CD2), J4.119 (CD19), and one or more of the monoclonal antibodies specific for an antigen on the surface of a breast or lung carcinoma as set forth in Table 4. Most preferably the monoclonal antibodies specific for an antigen on the surface of cells from a breast carcinoma used in a composition of the invention are one or more of 5E11, H23A, 6E7, RAR, BerEp4 and BRST1.

Detailed Description Paragraph Right (42):

In one embodiment, the tumor cells are metastatic tumor cells derived from epithelial cancers of the bronchi, mammary ducts, reproductive system, gastrointestinal tract and urogenital tract such as lung carcinoma, breast carcinoma, colon carcinoma, prostate carcinoma and bladder carcinoma.

Detailed Description Paragraph Right (81):

One currently used method for enriching for non-hematopoietic tumor cells is to use a negative selection technique with antibodies specific for CD45. The inventors have compared their antibody composition with anti-CD45 alone on the ability to enrich peripheral blood mononuclear cells for breast carcinoma tumor cells and have shown that the antibody composition of the invention enriches the tumor cells 10 fold (1 log) over anti-CD45 alone.

Detailed Description Paragraph Right (97):

Tetramers of anti-breast carcinoma antibodies as shown in Table 4 were combined with a progenitor enrichment cocktail (D2.10, UCHT1, MEM15, 3G8, ALB9, 80H3, J4.119, 6F10.3, T199, and optionally 8D2.2, T16 and FA60152, or 10F7MN, UCHT1, 32D12, MEM154, MEM15 or B13.9, T199, 6F10.3, J4.119, and optionally, 8D2.2, T16 and 1VC7) to produce a cocktail for breast carcinoma purging and debulking. Including the lineage depletion increases the degree of tumor purge over that seen with just anti-tumor antibodies alone (Table 7). Breast carcinoma cell lines were added to previously frozen marrow, peripheral blood leukapheresis or fresh bone marrow. Tumor cell purges were performed using the anti-breast carcinoma antibodies indicated in Table 7 with and without the standard lineage depletion (progenitor enrichment cocktail). The recovery of hematopoietic progenitors during lineage depletion is given in Table 8. Enrichment of progenitors was generally 50 to 100 fold.

Detailed Description Paragraph Right (99):

Cells from the CAMA breast carcinoma cell line were mixed with previously frozen bone marrow (BM) and processed with the enrichment antibody composition (D2.10, UCHT1, MEM15, 3G8, 80H3, J4119, 6F10.3, T199, 8D2.2, T16, FA6.152, and J33) in a one step magnetic depletion. The results shown in Table 9 demonstrates that the CAMA cells were enriched 2-3 log using the tumor enrichment antibody compositions.

Detailed Description Paragraph Right (100):

Cells from the CAMA breast carcinoma cell line were seeded into previously frozen peripheral blood mononuclear cells (PBMNC) and processed with the enrichment antibodies capable of binding to glycophorin A (2B7.1), CD2 (6710.3), CD14 (MEM15), CD16 (3G8), CD38 (T16), CD45 (J33) and CD66b (80H3) in a one step magnetic depletion. The results shown in Table 10 demonstrate that CAMA cells were enriched up to 4.5 log.

Detailed Description Paragraph Right (101):

Cells from the CAMA breast carcinoma cell line were seeded into previously frozen peripheral blood mononuclear cells (PBMNC) and processed with the enrichment antibodies capable of binding to glycophorin A (2B7.1), CD2 (6710.3), CD14 (MEM15), CD16 (3G8), CD38 (T16), CD45 (J33) and CD66b (80H3). The results were compared with the common method of negative selection, ie. the use of anti-CD-45 alone. The results shown in Table 11, demonstrates that there is close to a ten fold (1 log) greater enrichment using the antibody composition of the invention, over negative selection with CD45.

Detailed Description Paragraph Center (14):

Purging Breast Carcinoma Cells (BT20 or T47D Cells)

Detailed Description Paragraph Center (16):

Enrichment of Breast Carcinoma Cells in Bone Marrow

CLAIMS:

9. A process according to claim 8 wherein the epithelial cancer is selected from the group consisting of lung carcinoma, breast carcinoma, colon carcinoma, prostate carcinoma and bladder carcinoma.